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APPLICATION NUMBER: 60/491,695
FILING DATE: *August 01, 2003*
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Certified by



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Provisional Application Cover Sheet

Address to:
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Express Mail #:
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This is a request for filing a PROVISIONAL APPLICATION under 37 C.F.R. § 1.53(b)(3).

Docket Number: 02810	Type a plus sign (+) inside this box	+	
Inventor(s)/Applicant(s)			
Last Name	First Name	Middle Initial	Residence (City and either State or Foreign Country)
Sweeney	H	Lee	Philadelphia, PA
Morris	Carl		Philadelphia, PA
Kennedy	Ann		Wynnewood, PA
Title of the Invention (200 Characters Maximum) Use of BBI/ERIC for Treatment of Muscular Atrophy and Degenerative Muscle Disease			
Correspondence Address University of Pennsylvania Center For Technology Transfer 3160 Chestnut Street Suite 200			
City: Philadelphia		State: Pennsylvania	Zip Code: 19104 - 6283
Country: US			
Enclosed Application Parts (check all that apply)			
<input checked="" type="checkbox"/> Specification Number of pages: 5 <input type="checkbox"/> Small Entity Statement			
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Method of Payment (check one)			
<input type="checkbox"/> Our Check No. _____ is enclosed to cover the Provisional filing fees. A duplicate copy of this sheet is enclosed.		Provisional Filing Fee Amount (\$)	\$ 80.00
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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

No

Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

Signature:

Typed or Printed Name: H. Lee Sweeney

Date: 7/30/03

Additional inventors are being named on separately numbered sheets attached hereto.

PROVISIONAL APPLICATION FILING ONLY

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7. Description of Technology:

This technology involves new uses for Bowman-Birk Inhibitor Concentrate (BBIC). Preliminary results indicate that BBIC may be useful in treatment of disuse atrophy during periods of bedrest / inactivity and for prevention of muscle atrophy during spaceflight. Further, the preliminary data showing functional improvement of muscle during periods of disuse suggest a potential use of BBIC in treatment of degenerative muscle diseases.

1.) Grant Applications / manuscripts describing technology:

At this time, there has been no grant submission for the study of BBIC treatment of muscle atrophy or degenerative muscle disease.

2.) CV of Inventors

The current curriculum vitae for Dr. H. Lee Sweeney, Dr. Carl Morris, and Dr. Ann Kennedy are attached.

3.) Related publications

There not been any success in blocking disuse atrophy. The following papers are related to this.

Allen, D.L., Linderman, J.K., Roy, R.R., Bigbee, A.J., Grindeland, R.E., Mukku, V. and Edgerton, V.R., Apoptosis: a mechanism contributing to remodeling of skeletal muscle in response to hindlimb unweighting. *American Journal of Physiology* 273: C579-C587, 1997.

Allen, D.L., J.K. Linderman, R.R. Roy, R.E. Grindeland, V. Mukku, and V.R. Edgerton. (1997). Growth hormone/IGF-I and/or resistive exercise maintains myonuclear number in hindlimb unweighted animals. *J. Appl. Physiol.* 83(5): 1857-1861.

Allen, D.L., Monke, S.R., Talmadge, R.J., Roy, R.R. and Edgerton, V.R. Plasticity of myonuclear number in hypertrophied and atrophied mammalian skeletal muscle fibers. *Journal of Applied Physiology* 78: 1969-1976, 1995.

Allen, D.L., R.R. Roy, and V.R. Edgerton. (1999). Myonuclear domains in muscle adaptation and disease. *Muscle Nerve* 22: 1350-1360.

Criswell, D.S., Booth, F.W., DeMayo, F., Schwartz, R.J., Gordon, S.E., and M.L. Fiorotto. (1998). Overexpression of IGF-1 in skeletal muscle of transgenic mice does not prevent unloading-induced atrophy. *Am. J. Physiol.* 275 (Endocrinol. Metab. 38): E373-E379.

4.) Concise description of the technology

a.) Brief Description:

Preliminary experiments have shown that BBIC may be useful in treatment of muscle atrophy associated with disuse. A model system for disuse atrophy involves hindlimb suspension of mice by the tail, completely removing load from the hindlimb muscles, for a period of 14 days. Control experiments have shown soleus muscle mass reductions of 20 to 40% over the two-week suspension period, accompanied by similar declines in contractile force. Following a two-week suspension period, the soleus weights were compared between mice fed control food and food supplemented with BBIC. We observed an ~30% reduction in soleus muscle mass in suspended vs. non-suspended animals given the control food, while the BBIC-treated, suspended animals exhibited a ~21% loss of soleus muscle mass. Thus, our preliminary experiments with voluntary oral administration of Bowman-Birk's inhibitor suggest BBI/BBIC is a potential treatment for disuse atrophy. Further experiments will examine whether improved delivery, and therefore a greater quantity of BBIC, will further inhibit the muscle mass loss observed during hindlimb suspension.

A secondary potential use is in treatment and/or alleviation of symptoms associated with human degenerative muscle diseases. There are two distinct animal models of the human Duchenne muscular dystrophy (DMD) and limb-girdle muscular dystrophy (LGMD), the mdx mouse and the γ -sarcoglycan knock-out mouse, respectively. These two models represent different modes of pathogenesis, and in both cases, BBIC may slow the progression of the disease.

b.) Stage of Development

Currently, we are performing experiments to determine the potential for BBIC use to inhibit muscle atrophy. Following completion of the work, we will likely seek to publish the results in a peer-reviewed journal. Also, potential use of BBI/BBIC in human bed-rest trials is likely.

c.) Applications / Usages of the Technology

It is expected that BBIC will be useful in treatment of disuse atrophy in humans. The potential application of this technology could encompass anyone that is forced to become inactive for a period of greater than two weeks (e.g. casting of broken bone; patients requiring extended stays in hospitals). Also, astronauts involved in longer space flights under conditions of zero gravity could benefit from ingestion of BBI /BBIC.

The secondary application for use in degenerative muscle disease would be utilized as a potential treatment for patients with muscular dystrophy.

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d.) Closest known technologies

There is no current intervention in disuse atrophy. For human muscular dystrophy, steroids are the only treatment in use.

e.) Differences and Advantages over other technologies

Currently, there is no known ingested treatment for disuse atrophy. Electrical stimulation to maintain muscle tone is the only method that has any effect on inhibition of muscle loss during extended periods of inactivity. The ease of use and simplicity of BBI /BBIC treatment provides an enormous advantage over any potential gene therapy.

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Addendum to BBIC- Skeletal Muscle Atrophy Disclosure

Description of Technology:

This technology involves new uses for Bowman-Birk Inhibitor Concentrate (BBIC). Our results show BBIC inhibits muscle loss associated with unloading, such as during extended bedrest, casting, and/or spaceflight. This technology has been extended to include muscle atrophy associated with aging and chronic heart failure (CHF).

Brief Description of Technology:

The original disclosure noted the potential therapeutic use of Bowman-Birk inhibitor to counter the debilitating effects of skeletal muscle atrophy associated with extended periods of immobilization and disuse. This supplementary application describes two related usages of BBI/BBIC as a treatment against skeletal muscle atrophy.

First, as we age, our muscle mass and function declines markedly, with a 3-5% loss per decade starting at 30 years of age. By the time we reach 70 years old, the decline in strength is increased to almost 30% per decade (Nair, 1995). As we have found consumption of BBIC decreases disuse atrophy by ~50%, it is quite likely that BBIC will be effective in reducing the long-term muscle atrophy associated with aging. Currently, we are in the process of experimentally testing the effects of BBIC on aging mice.

Second, chronic heart failure (CHF) has been shown to cause significant skeletal muscle atrophy. CHF is recognized as a clinical disorder that dramatically reduces exercise capacity. Rehabilitation of the CHF patients is severely limited in intensity due to the loss of muscle mass and strength. This extends the period of recovery and reduces quality of life for these patients. By reducing the loss of skeletal muscle mass loss following CHF, BBIC may shorten the rehabilitation period and enable the patient to more quickly resume a normal lifestyle.

a.) Stage of Development

Currently, we have determined that BBIC consumption is able to inhibit the degree of muscle atrophy following disuse by approximately 50%. This result suggests that inhibition of protease activity may provide a protective mechanism against muscle atrophy resulting from other perturbations, such as aging and/or chronic heart failure. As such a preliminary aging study is under way to determine the effects of BBIC during aging. A group of 12-month-old mice have been randomly assigned to either a BBIC-feed group or a control-feed group. The muscle weight and strength of the two groups will be compared at 18- and 24-months of age (comparable to ~60 to 70 years of age in humans).

For the CHF study, we are currently working to develop an experimental protocol for heart failure in mice and submit the animal protocol to IACUC.

b.) Applications / Usages of the Technology

The original applications /usages can now be extended to include the aging population. Prevention or inhibition of atrophy associated with aging would be of great value over the next several decades. By slowing the effects of aging on muscle loss, the aging population would be able to remain more active and maintain quality of life for longer.

Further, consumption of BBIC to counter the skeletal muscle atrophy induced by chronic heart failure would accelerate recovery in these patients.

c.) Closest known technologies

For aging, the primary intervention is exercise, however this is difficult if there are compounding factors such as illness or injury. For CHF-induced atrophy, there is no direct treatment for the skeletal atrophy except slow recovery during rehabilitation. Calcium channel blockers or diuretics are used to treat the heart condition, not the skeletal muscle atrophy.

d.) Differences and Advantages over other technologies

Currently, there is no ingested treatment for skeletal muscle atrophy due to aging or CHF. Moderate exercise is the common therapy used to treat these disorders. However, as mentioned, this becomes difficult when other factors such as illness or injury prevent the patient from physical activity. Also, as stated previously, the ease of use and simplicity of BBI /BBIC treatment provides an enormous advantage over any potential gene therapy.

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